Remarks

The Examiner has rejected claims 1, 3-6, 8-11, 17 and 18 under 35U.S.C. 112 second paragraph as being indefinite in use of the word "active". This objection has been overcome by amendment. p53as and p53 have similar DNA binding functions and thus overlapping DNA growth regulating functions, even though they may not always be identical. As set forth on pages 8 and 9 of the specification, and as supported in Tables 1 and 2, it is however clear that both p53 and p53as both bind to the same known p53 binding sequence. This is now defined in the claims.

The rejection has now been rendered moot and should be withdrawn.

The Examiner has rejected claims 1, 3-6, 8-11, 17 and 18 as containing subject matter not sufficiently described in the specification (calling it new matter). Since all subject matter in the claims is specifically in the specification, a new matter rejection is clearly improper. The Examiner states that the "issue here is whether contemplating or making or using a non-p53 sequence for the purpose of providing a unique epitope at anywhere within p53as is disclosed in the specification. (emphasis added)" This statement is not understood. The applicants do not claim placing a unique epitope "anywhere" within p53as but only claim putting a unique epitope at the carboxy terminal end where the negative regulatory domain has been removed. Claim 1, for example, clearly says "...said p53as being different than p53 within the final 50 carboxy terminal amino acids of p53 so as to lack a negative regulatory domain of p53 for p53 specific DNA binding found within the last 50 amino acids at the p53 carboxy terminus and so as to provide an epitope within said p53as which gives rise to an antibody which is specific for p53as

protein only." It is grammatically clear that all modifications to p53 are in the final 50 amino acids. Not "anywhere". The claims have been amended to make it even clearer that the epitope is within the final 50 carboxy terminal amino acids and to make it clear that the epitope distinguishes p53as from p53, not necessarily from all other proteins in the universe.

The Examiner has rejected claim 16 under 35 U.S.C. 102 as being anticipated by Arai et al. This rejection should be withdrawn.

At the outset it should be pointed out that p53-M8 disclosed by Arai et al and the presently claimed p53as are not the same in that they do not have the same sequence or function. Sequentially, M8 is almost the same as p53as but for a change from Phe to Cys at position 132. M8 is thus **not** sequentially the same as p53 up to the final 50 carboxy terminal amino acids of p53 as required by the present claims. This is no minor change since functionality is radically affected by the single amino acid change within the body of p53. Changes in the regulatory sequence at the carboxy terminal end of p53 do not have such affects. p53as is an always active DNA binding protein. M8 is not a DNA binding protein at all. p53as acts in transformation suppression. M8 enhances malignant transformation. p53as forms tetromers. M8 is monomeric or forms dimers but not tetromers. p53as localizes in the nucleus. M8 appears in the nucleus and the cytoplasm. p53as and M8 are thus sequentially and functionally different. M8 clearly does not anticipate or suggest p53as. See the enclosed declaration of the inventor Dr. Molly Kulesz-Martin.

It is noted that large portions of p53as and p53-M8 have the same sequence; however, there is no suggestion in Arai et al that any particular portion of p53-M8 should be encoded into

a plasmid which portion is all or a part of the sequence specifically set forth in claim 16. In view of the present specification it is clear that a portion of the sequence set forth in claim 16 will raise an antibody response. Such a result is not suggested by nor obvious from any disclosure of Arai et al.

The Examiner's statement that the sequence could be as small as one or two amino acids is clearly not encompassed by nor possible within the claim limitations. No one or two amino acid peptide raises an antibody response as required by claim 16, since all one or two amino acid sequences occur naturally in the organism. In fact, it is generally believed that a peptide sequence must be at least 8 or 9 amino acids in length before an antibody response is possible. In the case that an eight amino acid sequence could raise such a response, which is unlikely, there are only ninety-one possible sequence portions of eight amino acids or longer within the peptide given in claim 16 that could even possibly raise an antibody response. There are only seventy-six of a length of ten or more that would be more likely to raise a response. Any or all such sequences can readily be tested by one skilled in the art for antibody response and if a response occurs the sequence could be used to distinguish p53 from p53as. The rejection is improper and should be withdrawn.

Claims 1, 3, 4 and 17 have been rejected under 35 U.S.C. 103 as being obvious over Han et al. in view of Sambrook et al. This rejection should be withdrawn. It is again reiterated that Han et al is interested in sequencing not function when considering incorporating portions of a DNA sequence encoding a p53 type protein. The Examiner has taken a quantum hindsight leap by then concluding that Han et al is somehow interested in function in conjunction with

misinterpretation

not in conjunction

incorporating such fragments into a plasmid. This is simply not true. Based upon hindsight, the Examiner then combines Sambrook et al. having no suggestion at all related to p53 sequences, or sequencing or function and somehow concludes that there is a fair teaching to make such a combination and then concludes that one should incorporate the entire p53as sequence into a plasmid (directly contrary to the specific teaching of Han et al) for purposes of determining function (again contrary to the purposes of Han et al.) The Examiner's attempted analogy to In re Kerkhoven is inappropriate. The purposes of Han et al. and Sambrook et al. are different and their organic compositions are clearly different and have different functions. This is contrary to all of the required tests of In re Kerkhoven. According to the Examiner's reasoning, incorporating any novel sequence into a plasmid would thus now be unpatentable no matter what the reason for incorporation. This is contrary to both logic and the law. The rejection is clearly improper and should be withdrawn.

Claims 5, 6, 8-11, and 18 have been rejected under 35 U.S.C. 103 as being obvious over Han et al. in view of Lee et al. Again this rejection should be withdrawn for reasons similar to those given with respect to the prior rejection. The Examiner continues to argue that Han et al. suggests incorporation of p53as into a plasmid for the purpose of studying function. Han et al. does no such thing. Han et al. incorporates fragments for the purpose of sequencing. Han et al. incorporates nothing at all into viruses for any purpose. Except based upon hindsight, there is no reason at all to combine Han et al. with Lee et al. Lee et al. is concerned with viral vectors but suggests nothing at all concerning a p53 sequence for any purpose and recognizes no purpose for incorporation of a p53 type sequence into a virus. (What would the function or

purpose for such incorporation be?) Again the Examiner misuses and misinterprets the authority of In re Kerkhoven. The purposes of Han et al. and Lee et al. are different and their organic compositions clearly different and have different functions. This is contrary to all of the required tests of In re Kerkhoven. The rejection should be withdrawn.

Claim 19 has been rejected under 35 U.S.C. 103 as being obvious over Arai et al in view of Lee et al. and Sambrook et al. Arai et al does not disclose or suggest the presently claimed sequence alone or within any vector, for reasons previously discussed, i.e. the Arai et sequence and function is different than the presently claimed sequence and function. Neither Lee et al nor Sambrook et al. suggest anything at all concerning any sequence remotely related to that presently claimed. The combination of these references therefore clearly cannot and does not suggest any of the present claims. The rejection is improper and should be withdrawn.

In view of the foregoing, is asserted that all objections and rejections have been overcome and all claims are in condition for allowance, which action is courteously requested.

Respectfully submitted,

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MLD/cah
cc: M. DeLellis
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Version with markings t show changes made

1. (amended) A plasmid containing a cDNA sequence which encodes a protein designated p53as, said p53as being [functionally equivalent in growth regulation to active] sequentially the same as wild type p53 [, said p53 and p53as being sequentially the same] up to the final 50 carboxy terminal amino acids of p53, said p53as being different than p53 within the final 50 carboxy terminal amino acids of p53 so as to lack a negative regulatory domain of p53 for p53 specific DNA binding found within the last 50 amino acids at the p53 carboxy terminus, which negative regulatory domain must be activated in p53 for p53 to have active DNA binding, said p53as and activated p53 binding to the same p53 DNA binding sequence AGGCATGCCT/AGGCATGCCT and said p53as being different than p53 within the final 50 carboxy terminal amino acids of p53 so as to provide an epitope within said p53as which gives rise to an antibody which is [specific for p53as protein only] reactive with the p53as but not with p53.